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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/578,603

05/04/2006

Jonathan Duffield

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EXAMINER

RUSSEL, JEFFREY E

ART UNIT

PAPER NUMBER

1654

MAIL DATE

DELIVERY MODE

01/28/2011

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/578,603	<b>Applicant(s)</b> DUFFIELD ET AL.	
	<b>Examiner</b> Jeffrey E. Russel	<b>Art Unit</b> 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 24 November 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-4,21 and 22 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4,21 and 22 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 04 May 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)         | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

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1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 24, 2010 has been entered.
2. In the Listing of Claims filed November 24, 2010, the status identifiers given for canceled claims 5-20 and 23-30 are incorrect. The correct status identifier is “(Canceled)”. Applicants are required to submit a corrected Listing of Claims in the response to this Office action using correct status identifiers.
3. Applicant's election of the invention of Group I, claims 1-4, 21, and 22, in the reply filed on September 8, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
5. Claims 1-4, 21, and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no original disclosure supporting the new definition of R<sub>4</sub> and R<sub>5</sub>, that these substituents can be “any organic substituents”. The new claim limitation is of such breadth as to embrace

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numerous and various types of substituents, such as organometallic compounds, polymers, and polycyclic rings, which would represent a radical departure from the types of chemical groups typically found in peptide backbones. There is no explicit, implicit, or inherent support in the original disclosure for the new claim limitation, and no indication in the original disclosure that Applicants contemplated such a wide range of organic substituents as forming part of their claimed compounds.

Applicants have not indicated where the original disclosure of the invention supports the new claim limitation. There is no original disclosure supporting the claim limitation in claim 4 that the sugar can be a dialdose, a ketoaldose, or a ketoaldose. Disclosure of a genus as broad as “carbohydrate” or “sugar” does not indicate that Applicants contemplated and had within their possession these three specific carbohydrates recited in claim 4, and does not provide explicit, implicit, or inherent support for the new claim limitation.

6. Claims 1-4, 21, and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The interpretation of the new definition of  $R_5$  in conjunction with the variable  $n$  in claim 1 is unclear. With  $R_5$  currently defined as any organic substituent, it would be possible to define  $n$  as being equal to the number of organic carbon atoms in a specific organic substituent, or, alternatively, regardless of the size of the specific organic substituent, it would be possible to define  $n$  as always being equal to 1. For example, for an organic substituent which is polyethylene glycol of formula  $(CH_2CH_2O)_{250}$ , it would be

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possible to define each carbon atom (including appropriate hydrogen and oxygen atoms) as being an organic substituent, and n would equal 500; it would be possible to define each ethylene glycol unit as being an organic substituent, and n would equal 250; or it would be possible to define the entire polyethylene glycol molecule as being the organic substituent, in which case n would equal 1. Consistent rules of claim interpretation are not possible. The Markush group recited in claim 4 is unclear because neutral-sugars, acidic-sugars, aldoses, ketoses, cyclic sugars, dialdoses, diketoses, and ketoaldoses are not species of the amino sugar, deoxy sugar, or sialic acid sugar being defined in the claim. The listed members of the Markush group are not specific types of the amino sugars, deoxy sugars, or sialic acid sugars being defined in the claim; rather, each represents a genus of compounds which overlaps the amino sugars, deoxy sugars, and sialic acid sugars being defined in the claim. It is not clear if the claim should be interpreted as embracing, e.g., only those neutral-sugars which are also amino sugars, deoxy sugars, or sialic acid sugars, or if the claim should be interpreted as embracing, e.g., neutral sugars including those which are not amino sugars, deoxy sugars, or sialic acid sugars.

7. Claims 1-4, 21, and 22 are objected to because of the following informalities: In claim 1, in the definition of R<sub>3</sub>, line 4 of the definition, the comma after the deleted word “arylalkyl” also needs to be deleted. Appropriate correction is required.

8. Claims 1-4, 20, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Wagner et al (U.S. Patent No. 3,971,736). In Example 9, Wagner et al teach a compound present in the filtrate at column 13, line 7, which is 3,4,6-tri-O-acetyl-2-deoxy-2-

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acetamidoglucopyranosyl-DPhe-Pro-Phe-Phe-Val-DLeu-OEt. Treatment of the resin with methanol-triethylamine results in removal of the compound from the resin on which it has been synthesized in the form of an ethyl ester (see column 3, lines 13-22) without removal of the acetyl groups from the 2-deoxy-2-acetamidoglucopyranosyl substituent. Note that every available hydroxyl group present in the 2-deoxy-2-acetamidoglucopyranosyl substituent is modified by acetylation, which acetyl groups are not removed until the NaOH treatment at column 13, lines 8-10. The compound of Wagner et al corresponds to Applicants' Formula I in which  $m=1$ ;  $R_1$  is 3,4,6-tri-O-acetyl-2-deoxy-2-acetamidoglucopyranosyl;  $R_2$  is NH;  $R_3$  is a linker which is a combination of alkyl and aryl groups (i.e., the phenyl-CH<sub>2</sub>-CH from the DPhe residue); and  $NH-R_4-C(=O)-NH-(R_5)_n-CO$  is Pro-Phe-Phe-Val-DLeu. In view of the similarity in structure between the compound of Wagner et al and Applicant's claimed compounds, inherently the compound of Wagner et al will have increased stability in the presence of peptidases and proteases, increased thermal stability, increased dimer half-life, increased bioavailability, and increased plasma half-life in comparison to a non-glycosylated analog, and inherently the 3,4,6-tri-O-acetyl-2-deoxy-2-acetamidoglucopyranosyl will serve as a stable surrogate for a specific amino acid residue to the same extent claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the compound of Wagner et al and Applicants' claimed compounds to shift the burden to Applicants to provide evidence that their claimed compounds are unobviously different than the compound of Wagner et al. Note that a difference in intent or descriptive terminology does not impart novelty or nonobviousness to product claims where the claimed product is otherwise taught by the prior art.

9. Applicant's arguments filed November 24, 2010 have been fully considered but they are

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not persuasive.

Concerning the rejection of claim 4 under 35 U.S.C. 112, first paragraph, Applicants' arguments are convincing that aldoses and cyclic sugars are supported, e.g., by page 10, lines 8-9 and 25-26 of the specification. The examiner maintains his position that dialdoses and ketoaldoses are not supported by the original disclosure of the invention, and now believes that diketoses also are not supported by the original disclosure of the invention. Contrary to Applicants' arguments, "dialdoses", "diketoses", and "ketoaldoses" are not explicitly recited in the original disclosure. Dialdoses, diketoses, and ketoaldoses are not implicitly disclosed in the application as originally filed - given the vast size of the genus of carbohydrates, sugars, and saccharides, and in view of the relatively uncommon presence in the art of dialdoses, diketoses, and ketoaldose, it would not be understood by one skilled in the art that Applicants were specifically contemplating dialdoses, diketoses, and ketoaldose as forming part of their disclosure of carbohydrates, sugars and/or saccharides. Dialdoses, diketoses, and ketoaldoses are not inherently disclosed in the application as originally filed - given the vast size of the genus of carbohydrates, sugars, and saccharides, and given the disclosure of numerous species which are not dialdoses, diketoses, or ketoaldoses, one skilled in the art would not conclude that Applicants inherently disclosed three relatively rare unnamed species. It is a common concept in the patent law that a genus does not necessarily constitute a written description of every species encompassed by the genus. See MPEP 2163(I)(B), first paragraph, and (II)(A)(3)(b). It is also a common concept in the patent law that a species does not necessarily provide written descriptive support for a genus although it can still anticipate claims drawn to the genus. See MPEP 201.11(I)(B), last two paragraphs. Anticipation is a different legal concept than written

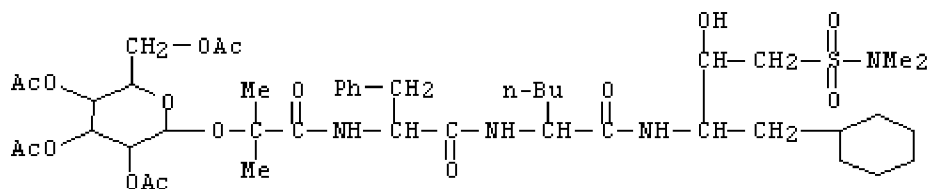
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description, and a finding of anticipation does not necessitate a conclusion that a generic disclosure constitutes a written description of the anticipatory species.

Concerning the rejection under 35 U.S.C. 112, second paragraph, and the interpretation of the  $R_4$  and  $R_5$  groups and the variable  $n$ , the amendment to the claim, while negating the previous rejection, raises new issues as to how the claim is to be interpreted. Applicants are requested to review the rejection under 35 U.S.C. 112, second paragraph, in the previous Office action. It is possible that Formula I itself, in addition to the definitions of  $R_4$  and  $R_5$ , is incorrect and/or unclear. It is possible that  $NH-R_4-C(=O)$  and  $NH-R_5-C(=O)$  should represent any amino acid (natural or otherwise), and that the Formula should read, in part,  $(NH-R_5-C(=O))_n$  rather than  $NH-(R_5)_n-C(=O)$ . Note that if the Formula in the claims needs correction and/or clarification, the Formulas throughout the specification will also need analogous correction and/or clarification.

The anticipation rejection based upon Wagner et al (U.S. Patent No. 3,971,736) is maintained. While Applicants have amended the definition of  $R_3$  to delete “arylalkyl”, the claimed definition of  $R_3$  still recites that the linker can be “composed of... in any combination... alkyl... aryl”, and thus still embraces the corresponding arylalkyl group present in the compound of Wagner et al.

10. GB 2,200,115 is cited as art of interest, in particular for its teaching of the compound at page 46, Example 52. Chemical Abstracts provides the following structure for the compound:





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Note, however, that the reference's compound does not comprise a carboxylic acid group or an ester group at the C-terminus of the dipeptide. Further, the group attached to the carboxy terminus of the norleucine residue is not described as acting as a pro-drug masking/leaving group, and does not appear as though it would act as a pro-drug masking/leaving group.

Accordingly, the reference's compound is not deemed to anticipate or render obvious

Applicants' claims.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:00 A.M. to 5:30 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (571) 272-0562. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jeffrey E. Russel/

Primary Examiner, Art Unit 1654

JRussel

January 26, 2011